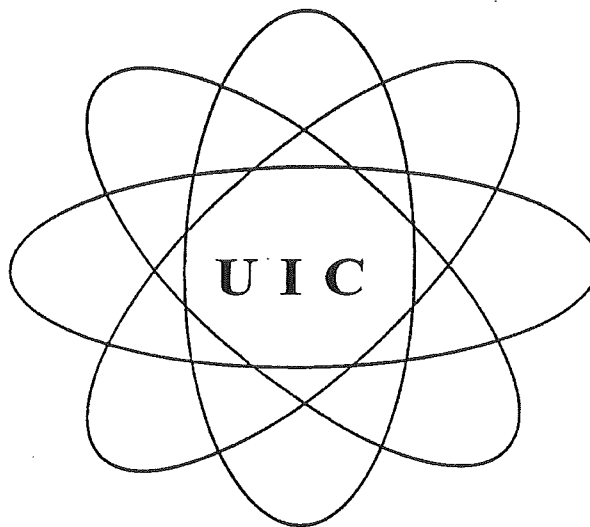


COURSE NOTES IN MEDICAL RADIATION BIOLOGY



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SECTION IV: ACCUTE EFFECTS OF WHOLE BODY IRRADIATION**LESSONS FROM CHERNOBYL**

On April 26, 1986, the world's most serious nuclear accident occurred at the Chernobyl Nuclear Power Station in the Soviet Union. Approximately 185×10^{10} MBq (50 MCI), or 3 to 5%, of the fuel inventory was released along with an equal amount of radioactivity in the form of noble gases. Twenty-five percent was released instantaneously and the remainder over approximately ten days.

The immediate medical response involved five phases:

1. assessment (thermal & radiation exposure)
2. containment
3. reduction of exposure to individuals at risk
4. dosimetry of exposed individuals
5. medical intervention

1. ASSESSMENT OF RADIATION DOSE

There are two basic approaches, physical and biological dosimetry.

- a. physical (of limited value)

environmental monitors, film badges (At Chernobyl most environmental monitoring devices were either destroyed or unrecoverable.)

- b. biological dosimetry (of great value)

lymphocytes levels, granulocytes levels, dicentric chromosomes in spontaneously dividing hematopoietic cells.

interval of onset of nausea or emesis

analysis of sodium²⁴ indicated the absence of detectable neutron component in the radiation exposure.

2. THE MEDICAL RESPONSE

The major elements in the medical response to a radiation accident "involve the treatment of skin burns and measures designed to correct or reverse bone marrow failure and gastrointestinal tract injury".

Immediate response involves supportive measures such as protective isolation, gastrointestinal tract decontamination, antibacterial, antifungal and antiviral therapy and transfusion of blood products.

- a. **Infection prophylaxis:**

For patients receiving greater than 1 Gy of radiation, multiple drugs were used both therapeutically and prophylactically. Patients were kept in isolation and some were maintained in relatively sterile laminar airflow environments. Oral antibiotics were given to modify the endogenous gastrointestinal tract flora and to decrease the likelihood of infection. Systemic antibiotics were used in febrile patients with granulocytopenia. Radiation-induced activation of herpes simplex virus was a major problem in most individuals; this complication responded to

treatment with acyclovir.

b. Transfusion Support:

Transfusion of RBC's and platelets was used extensively. The latter was obtained from multiple random donors as well as by thrombocytapheresis from a single donor.

c. Bone Marrow Transplantation:

The consideration of candidates to receive bone marrow transplants was complex:

- at risk due to significant exposure (3 Gy)
- exclude those who will probably die from other nonhematopoietic toxic damage
- HLA typing to determine donor availability (related or nonrelated donors)
- Possible use of fetal liver cells which is rich in hematopoietic stem cells. These cells are not likely to cause a graft vs. host reaction.

3. LESSONS LEARNED

- a. Intensive supportive care was associated with a high rate of survival in most individuals receiving less than 6 Gy of whole body radiation.
- b. Such measures as the use of systemic antibiotic, gastrointestinal tract decontamination and platelet transfusions can save lives.
- c. Bone marrow transplantation can only save a small proportion of victims of radiation accidents because irreversible damage to other organs is likely to limit the success of this procedure. Availability of international HLA-typed volunteer donor registries and the ability to remove T-lymphocytes from the graft may help this approach.

WHOLE-BODY EFFECTS OF IONIZING RADIATION

- **ACUTE: Up to Six Months**

e.g. Dry Mouth, diarrhea, erythema

- **CHRONIC: Occur six months or longer**

e.g. Stricture of Esophagus, cancer induction

RADIATION SYNDROMES SOURCES:

- Atomic Warfare
- Accidents: Lab., Nuclear Reactors
- Planned Total Body Irradiation

RADIATION SYNDROMES

- Central Nervous System (CNS)
- Gastrointestinal (GI)
- Hematopoietic (Bone Marrow)

FACTORS WHICH MAY INFLUENCE RADIATION RESPONSE

- Radiation Source

- Total Dose
- Volume Irradiated
- Prior Injury
- General Condition

RADIATION LETHALITY

- LD 50/l CNS: Death
- LD50/7 GI: Death
- LD50/30 BM: Death

RADIATION SYNDROMES:

TREATMENT

- Observation
- Treatment of Symptoms
- Sterilized Isolation & Feeding
- Bone Marrow Transplant???

A. ACUTE RADIATION SYNDROME

1. Definitions

- a. High Dose > 1Gy (100 rads)
- b. Acute < 1 hour
- c. Total Body or Large Volume Exposure
- d. External Irradiation (not internal deposition)

2. Clinically Observable Syndromes

- a. Prodrome: Clinical Syndrome + Latent Period + Manifest Illness
- b. Hematologic } Recovery Manifest Illness
- c. Gastrointestinal (GI) } Death
- d. Central Nervous System (CNS) Death

B. PRODROMAL SYNDROME >1 Gy (100 rads)

1. Clinical Symptoms

- a. Onset: minutes (high doses) + hours (lower doses)
- b. Nausea }
- c. Vomiting } i.e. CNS Syndrome
- d. Diarrhea }
- e. Lymphocyte depletion
- f. Duration: hours + weeks
- g. Onset:
 - Minutes (High Dose) : > 2.5 Gy (250 rads)
 - Hours (Lower Dose) : 1-2 Gy (100-200 rads)

2. Latent Period

- a. Apparent return to normal health
- b. No overt sign of radiation sickness
- c. Duration:

- hours > 100 Gy (10,000 rads)
- week 1-5 Gy (100-500 rads)
- d. Progression of sub-clinical radiation damage.
- e. Duration:
 - High Dose--hours
 - Lower Dose--week

C. HEMATOLOGICAL SYNDROME (BONE MARROW SYNDROMA) (1-10 Gy; 100-1,000 rads)

1. **Clinical symptoms**

- a. mild prodrome (hours + days)
- b. latent period (up to 4 weeks)
- c. manifest illness: leukopenia. + pancytopenia.

2. **Cause of Death**

yes Starts 2-4 week, complete < 6 months

a. Recovery

no Hemorrhage & Infection

Electrolyte Imbalance & Dehydration

b. Exposure Death

- 300-500 R 4-6 weeks
- 500-1,000 R 2 weeks

c. Threshold for death – 2Gy (200 rads) LD 50/60: 450R or 2.5-3 Gy (250-300 rad.)

- No one has survived exposures of 10 Gy (1,000 rads) without medical intervention or > 12 Gy (1,200 rads) with medical intervention (bone marrow transplant).



D. GASTROINTESTINAL (GI) SYNDROME (= 10-50 Gy; 1000-5000 rads)

1. Clinical Symptoms

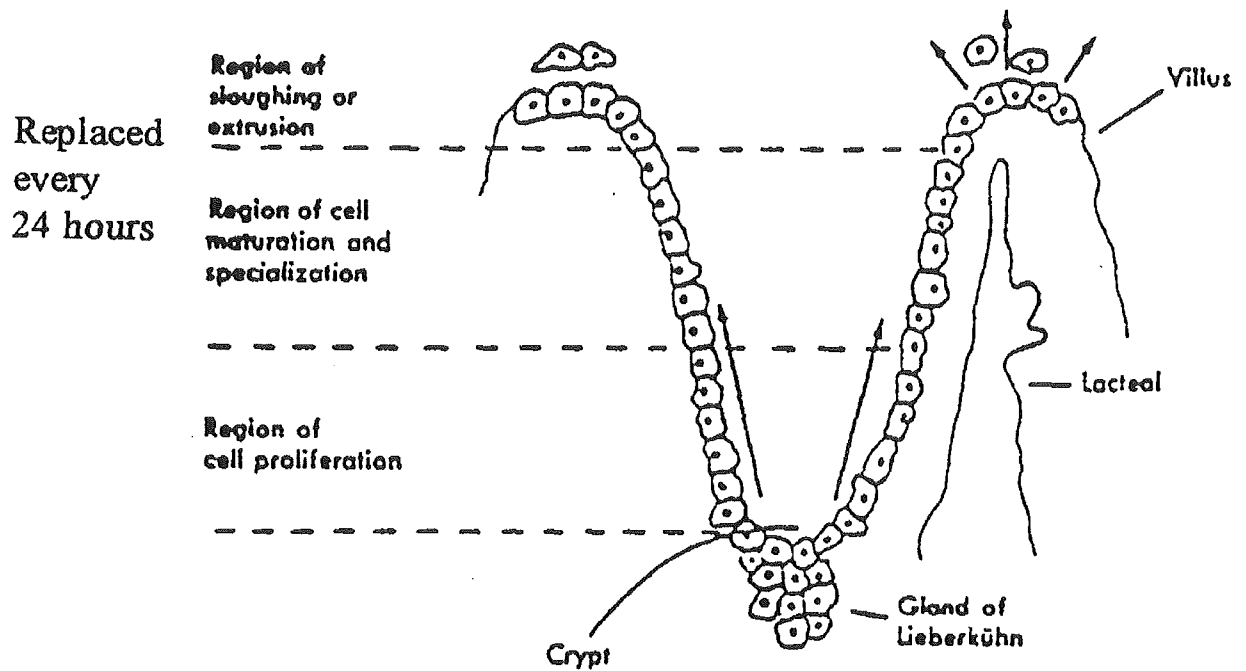
a. Prodrome

- within hours, explosive
- vomiting, diarrhea, cramps (severe at high doses)

b. Latent Period (3-5 days)

c. Manifest Illness: (threshold 600 R)

- severe hematologic response plus loss of GI integrity



2. Cause of death: 4-10 days without medical support; = 2 weeks with medical support
 - a. Infection + communication of bacteria and blood also leukocytes
 - b. Severe Electrolyte Imbalance
 - c. Severe Dehydration
 - d. secondary to surface area with shortened, flatter villi
 - e. Shock
 - f. Irreversible damage to GI germinal layer and bone marrow

2. CENTRAL NERVOUS SYSTEM (CNS) SYNDROME (>50 Gy; 5000 rads)

1. Clinical Symptoms
 - a. Nausea and vomiting (within minutes)
 - b. Nervous, confused, possibly loss of consciousness
 - c. Latent period (6-12 hours)
 - prodrome subsides
2. Manifest Illness:
 - a. return of prodrome (violent)
 - b. loss of muscle coordination, difficult breathing and seizures
 - c. shock coma death
3. Medically unalterable course
4. Cause of Death (hours - few days)
 - a. Elevated fluid level in the brain: intracranial pressure
 - b. Acute inflammatory changes in blood vessels
 - vasculitis
 - meningitis
 - c. Hematological and gastrointestinal syndromes do not occur because patient dies before they can be expressed

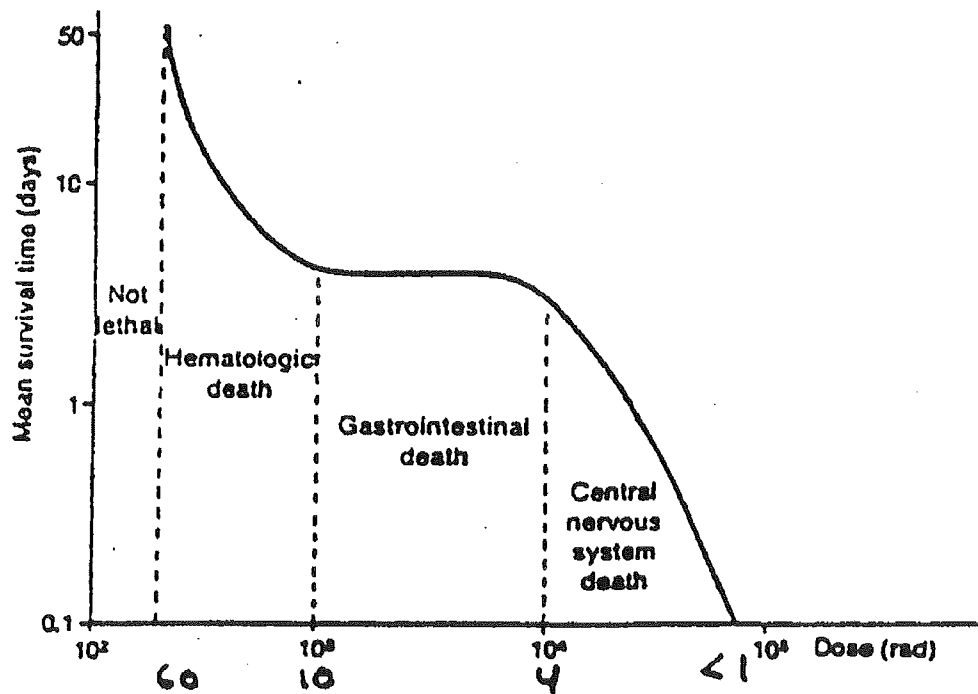
3. Summary of Acute Radiation Syndrome

1. Overview

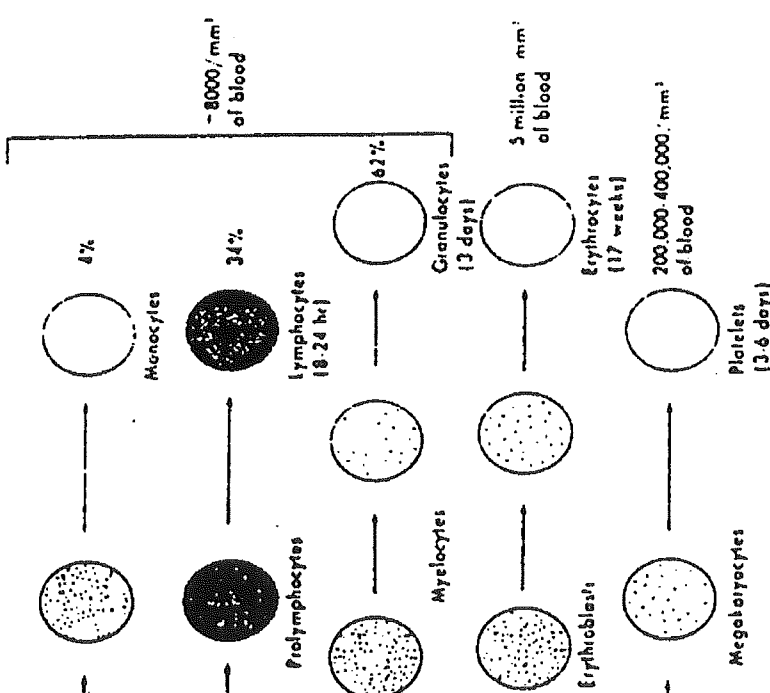
Stage	Dose Gy (rad)	Mean survival time (days)	Clinical signs and symptoms
Prodromal	>1 (100)		Nausea, vomiting, diarrhea
Latent	1 to 100 (100 - 10,000)	10 to 60	None
Hematologic	2 to 10 (200 - 1000)	4 to 10	Nausea, vomiting, diarrhea, leukopenia, hemorrhage, fever, infection
Gastrointestinal	10 to 50 (1000 - 5000)	0.5 to 3	Same as hematologic: electrolyte imbalance, lethargy, fatigue
Central nervous system	>50 (5000)		same as GI, ataxia, edema, meningitis

4. Dose Response Relationships

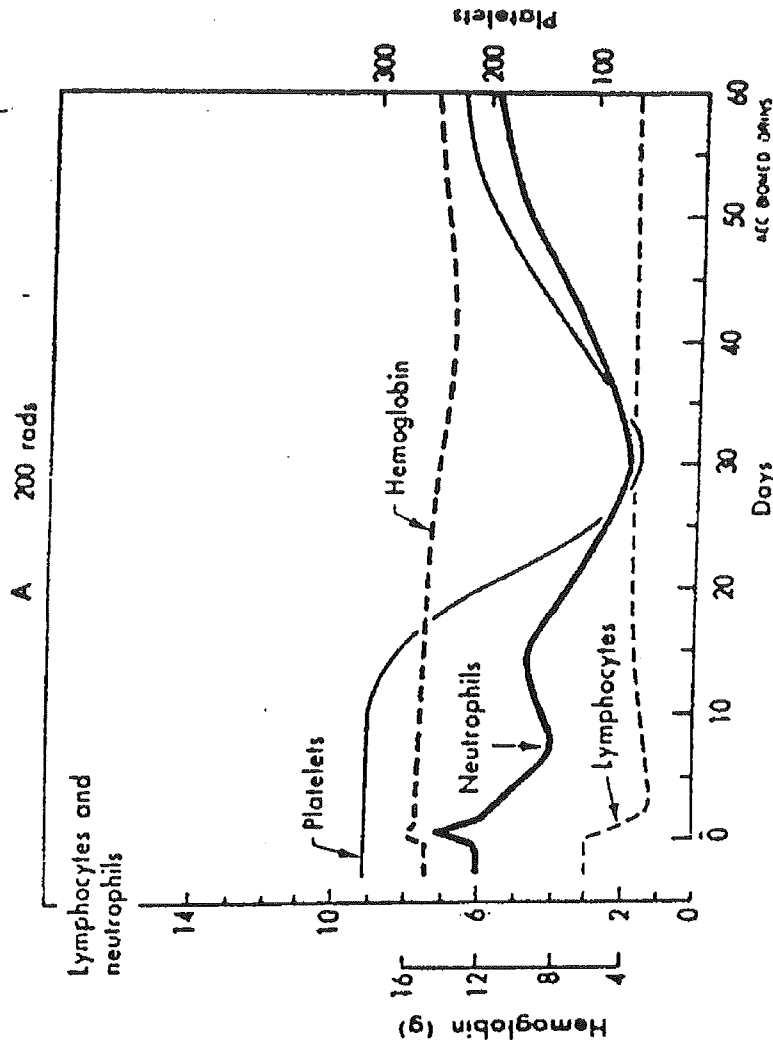
a. Dose vs. Syndrome (Cause of Death)



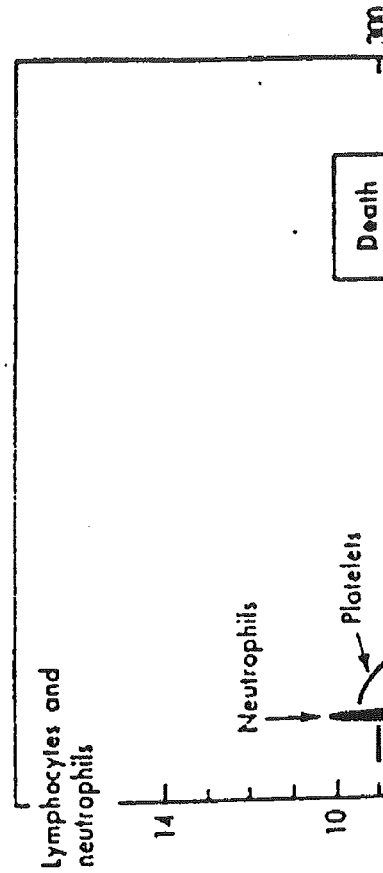
Radiosensitivities and Profiles



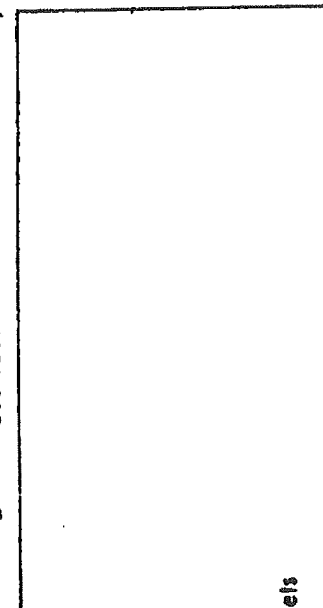
Black spheres represent very radiosensitive stages; white spheres are radioresistant cells. The lifetimes of mature blood



C 450 rads



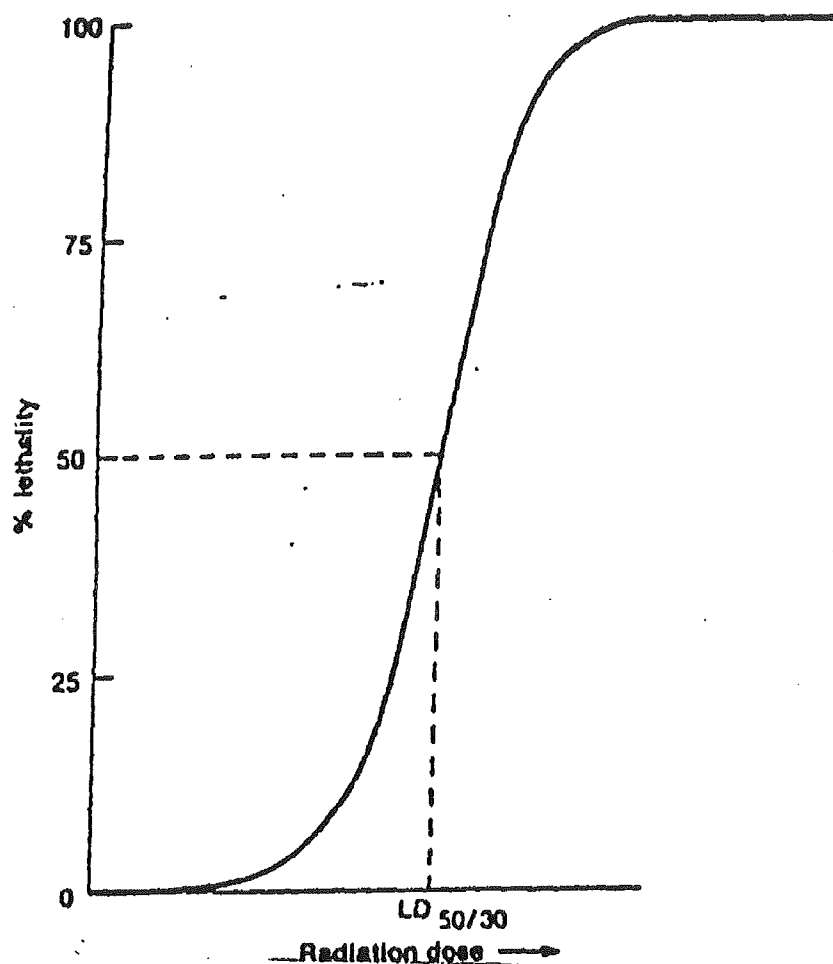
B 300 rads



G. LD_{50/30}1. Definitions (LD_{50/30}):

a. *Acute dose of radiation to the whole body that will result in death within 30 days to 50% of a population so irradiated.*

2. Examples



LD_{50/30} for various species

following whole-body x-radiation

Species	LD _{50/30} Gy (rad)
Pig	2.5 (250)
Dog	2.75 (275)
Guinea pig	3 (300)
Monkey	4.25 (425)
Opposum	5.1 (510)
Mouse	6.2 (620)
Goldfish	7 (700)
Hamster	7 (700)
Rat	7.1 (710)

Rabbit	7.25 (725)
Gerbil	10.5 (1050)
Turtle	15 (1500)
Newt	30 (3000)

Summary of Pertinent Conclusions

- The prodromal syndrome varies in time of onset severity and duration. At doses close to the LD₅₀ the principal symptoms of the prodromal syndrome are anorexia, nausea, vomiting and easy fatigability.
- Immediate diarrhea, fever or hypertension indicates a supralethal exposure.
- The cerebrovascular syndrome- results from whole-body exposure about 10,000 rads (100 Gy) of γ -rays and results in death in 30 min to hours. The cause of death may be changes in permeability of small blood vessels in the brain.
- The gastrointestinal syndrome results from whole-body exposure about 1000 rads (10 Gy). Death occurs in about 9 days in humans because of depopulation of the epithelial, lining of the gastrointestinal tract.
- The hematopoietic syndrome results from whole-body exposure 300 to 800 rads (3 to 8 Gy). The radiation sterilizes some or all of the mitotically active precursor cells. Symptoms result from lack of circulating blood elements 3 weeks or more later.
- The LD₅₀ for humans (i.e., the dose that would be lethal to 50% of population) is 300 to 400 rads (3 to 4 Gy) for young adults without medical intervention. It may be less for the young or the old.
- Some individuals who would otherwise die may be saved by antibiotics, platelet infusions or bone marrow transplants.
- In animals the LD₅₀ can be raised by a factor or two by appropriate treatment including careful nursing and antibiotics.